NATIONAL GUIDELINE CLEARINGHOUSE™ (NGC™) GUIDELINE SYNTHESIS

SCREENING FOR PROSTATE CANCER

Guidelines

1. American College of Preventive Medicine (ACPM). Screening for prostate cancer in American men. Am J Prev Med 1998 Jul;15(1):81-4 [43 references].
2. American Urological Association, Inc. (AUA). Prostate specific antigen: Best practice policy. Baltimore (MD): American Urological Association, Inc., 1999. 30 p [130 references].
3. Singapore Ministry of Health (MOH). Prostate cancer. Singapore: Ministry of Health (Singapore); 2000 May. 49 p. (Ministry of Health Singapore clinical practice guidelines; no. 3/00). [168 references]
4. American Cancer Society (ACS). Recommendations from the American Cancer Society Workshop on Early Prostate Cancer Detection, May 4-6, 2000 and ACS guideline on testing for early prostate cancer detection: update 2001. CA Cancer J Clin 2001 Jan-Feb;51(1):39-44 [181 references].
5. U.S. Preventive Services Task Force (USPSTF). Screening for prostate cancer: recommendations and rationale. Ann Intern Med 2002 Dec 3;137(11):915-6 [8 references].

INTRODUCTION:

A direct comparison of ACPM, AUA, Singapore MOH, ACS and USPSTF guidelines on screening for prostate cancer is provided in the following tables. The supporting evidence is classified and identified with the major recommendations from the Singapore MOH and USPSTF. The definitions of their rating schemes are included in the last rows of Table 2.

Following the content comparison, areas of agreement and differences among the guidelines are discussed.

Abbreviations:

- ACPM, American College of Preventive Medicine
- ACS, American Cancer Society
- AUA, American Urological Association
- DRE, digital rectal examination
- PSA, prostate specific antigen
- MOH, Ministry of Health
- USPSTF, U.S. Preventive Services Task Force

TABLE 1: COMPARISON OF SCOPE AND CONTENT	
ACPM (1998 Jul)	*Objective:* To present a practice policy statement on screening for prostate cancer in Am men. *Interventions and Practices Considered:* • DRE • Serum tumor markers (e.g., PSA) • Transrectal ultrasound *Target Population:* American men 40 years of age and older
AUA (1999)	*Objective:* To provide current information on the use of PSA testing for 1) early detection prostate cancer, 2) assistance in pretreatment staging, and 3) the post-treatm monitoring and management of men with this disease. *Interventions and Practices Considered:* • DRE • PSA • Transrectal ultrasound *Target Population:* • Asymptomatic men age 50 or over with an anticipated life expectancy of more years • Asymptomatic men age 40 to 50 years old with a family history of prostat or African-American ethnicity with an anticipated life expectancy of 10 or years
Singapore MOH (2000)	*Objective:* To provide recommendations for the management of patients with prostate ca *Interventions and Practices Considered:* • DRE • PSA Interventions for the diagnosis, management and treatment of prostate ca also presented in the guideline. Transrectal ultrasound with and without b discussed in the context of diagnosis rather than screening. *Target Population:* Asian men, 40 years of age and older with the risk factor of having a first degr relative with prostate cancer at a young age (< 60 years)

ACS (2001)	*Objectives:* • To update the 1997 American Cancer Society guideline pertaining to pros cancer screening. • To offer recommendations to health care professionals and the public for decision-making related to early detection of prostate cancer. *Interventions and Practices Considered:* • DRE • PSA *Target Population:* • Men aged 50 years and older who have a life expectancy of at least 10 ye younger men who are at high risk for prostate cancer • Men aged 45 years and older of Sub-Saharan African descent or with firs relative diagnosed at a young age • Men 40 and older with multiple first-degree relatives diagnosed with prost cancer at an early age
USPSTF (2002)	*Objectives:* • To summarize the current U.S. Preventive Services Task Force (USPSTF recommendations on screening for prostate cancer and the supporting sc evidence • To update the 1996 recommendations contained in the *Guide to Clinical Preventive Services*, second edition *Interventions and Practices Considered:* • DRE • PSA *Target Population:* • Men aged 50-70 years who are at average risk • Men over age 45 who are at increased risk (African American men and m a family history of a first-degree relative with prostate cancer)

TABLE 2: COMPARISON OF RECOMMENDATIONS FOR PROSTATE CANCER SCREENING	
ACPM (1998 Jul)	**Routine screening** The American College of Preventive Medicine (ACPM) recommends against r

	population screening with DRE and PSA. **Targeted screening/Informed decision-making** Men age 50 or older with a life expectancy of greater than 10 years should be information about the potential benefits and harms of screening and limits of c evidence and should be allowed to make their own choice about screening, in consultation with their physician, based on personal preferences. Methods and for helping patients review this information are available; however, the ACPM recommends further research be conducted in optimizing the process of patie education and informed consent.
AUA (1999)	**Targeted screening** Early detection of prostate cancer should be offered to asymptomatic men 50 age or older with an estimated life expectancy of more than 10 years. It is reas to offer testing at an earlier age to men with defined risk factors, including mer first-degree relative who has prostate cancer and African American men. **Informed decision-making** Decisions regarding early detection of prostate cancer should be individualize benefits and consequences should be discussed with the patient before PSA t occurs. Not all men over age 50 are appropriate candidates for screening effo this disease. Ideally, physicians should consider a number of factors including age and comorbidity as well as preferences for the relevant potential outcome organizations have even recommended that informed consent should be obtai to PSA testing. **Screening tests** PSA testing detects more tumors than does DRE, and it detects them earlier. the most sensitive method for early detection of prostate cancer uses both DR PSA. Both tests should be employed in a program of early prostate cancer de Evidence from three uncontrolled studies that allow a direct comparison of the PSA and DRE suggests that combining both tests improves the overall rate of cancer detection when compared with either test alone. The value of serial determinations of PSA or serial DRE in patients with a normal initial examinati unknown. There is evidence that serial PSA determinations lead to a decrease detection of pathologically advanced disease. Transrectal ultrasonography is not a useful test for early prostate cancer detec adds little to the combination of PSA and DRE.
Singapore MOH (2000)	**Routine screening** At present, population-based screening is not recommended among Asians. (***Level Ia***) **Targeted screening** All males above 40 years of age with the risk factor of having a first degree rel with prostate cancer at young age (younger than 60 years) may be screened. ***Practice Point***) **Screening tests:**

	Prostate specific antigen The appropriate threshold prostate specific antigen level for the detection of ca the prostate is 4.0 ng/ml. (***Grade B, Level IIb***) Clinically significant cancers are detected by PSA testing. (***Grade B, Level IIa*** Prostate specific antigen-based screening has induced a stage migration but c preliminary indications of improved survival are available. (***Grade C, Level IV***) The ratio of free to total prostate specific antigen levels is recommended as th sensitivity and specificity of levels at 2 to 10 ng/ml for detecting cancer of the p is higher. (***Grade B, Level IIa***) However, the optimal cut-off level is still being investigated. *Digital rectal examination* Digital rectal examination is recommended as the combination of DRE and PS enhances early prostate cancer detection. (***Grade B, Level IIa***)
ACS (2001)	**Targeted screening/Screening tests/Informed decision-making** The American Cancer Society (ACS) recommends that both the PSA test and should be offered annually beginning at age 50, to men who have a life expect at least 10 years. Men at high risk should begin testing at age 45. Information be provided to patients about benefits and limitations of testing. Specifically, p testing, men should have an opportunity to learn about the benefits and limitat testing for early prostate cancer detection and treatment. High-risk groups include men of African descent (specifically, sub-Saharan Afr descent) and men with a first-degree relative diagnosed at a young age. Risk increases with the number of first-degree relatives affected by prostate cancer
USPSTF (2002)	**Routine screening** The U.S. Preventive Services Task Force (USPSTF) concludes that the evider insufficient to recommend for or against routine screening for prostate cancer prostate specific antigen (PSA) testing or digital rectal examination (DRE). **I recommendation**. *The USPSTF found good evidence that PSA screening can detect early-stage cancer but mixed and inconclusive evidence that early detection improves hea outcomes. Screening is associated with important harms, including frequent fa positive results and unnecessary anxiety, biopsies, and potential complications treatment of some cancers that may never have affected a patients health. Th USPSTF concludes that evidence is insufficient to determine whether benefits outweigh harms for a screened population.* **Clinical Considerations** • Prostate specific antigen (PSA) testing and digital rectal examination (DR effectively detect prostate cancer at early pathologic stages. There is insu evidence, however, that the currently available treatments (radical prosta radiation therapy, or hormonal therapy) reduce morbidity and mortality fro

	prostate cancer. Therefore, the benefit of screening for and treating early cancer is unknown. **Informed decision-making/Targeted screening/Screening tests/Screening frequency** **Clinical Considerations** • Despite the absence of firm evidence of effectiveness, some clinicians ma perform screening for other reasons. Given the uncertainties and controv surrounding prostate cancer screening, clinicians should not order the PS without first discussing with the patient the potential but uncertain benefits (reduction of morbidity and mortality from prostate cancer) and the possib (false-positive results, unnecessary biopsies, and possible complications treatment) of prostate cancer screening. Men should be informed of the g the evidence, and they should be assisted in considering their personal preferences and risk profile before deciding whether to be tested. • If early detection improves health outcomes, the population most likely to from screening will be men aged 50-70 years who are at average risk, an over age 45 who are at increased risk (African American men and men w family history of a first-degree relative with prostate cancer). Benefits may smaller in Asian Americans, Hispanics, and other racial and ethnic groups have a lower risk of prostate cancer. Older men and men with other signif medical problems who have a life expectancy of fewer than 10 years are to benefit from screening. • PSA testing is more sensitive than DRE for the detection of prostate canc screening with the conventional cut-point of 4.0 ng/ml detects a large maj prostate cancers; however, a significant percentage of early prostate can 20%) will be missed by PSA testing alone. Using a lower threshold to defi abnormal PSA detects more cancers at the cost of more false positives a biopsies. • The yield of screening in terms of cancer detected declines rapidly with re annual testing. If screening were to reduce mortality, biennial PSA screer could yield as much benefit as annual screening.
Rating Scheme	
ACPM (1998 Jul)	Not applicable
AUA (1999)	Not applicable
Singapore MOH (2000)	**Levels of Evidence** Level Ia: Evidence obtained from meta-analysis of randomised controlled trials Level Ib: Evidence obtained from at least one randomised controlled trial. Level IIa: Evidence obtained from at least one well-designed controlled study w

	randomisation. Level IIb: Evidence obtained from at least one other type of well-designed qua experimental study. Level III: Evidence obtained from well-designed non-experimental descriptive such as comparative studies, correlation studies and case studies. Level IV: Evidence obtained from expert committee reports or opinions and/or experiences of respected authorities. **Grades of Recommendation** Grade A (evidence levels Ia, Ib): Requires at least one randomised controlled part of the body of literature of overall good quality and consistency addressin specific recommendation. Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted cl studies but no randomised clinical trials on the topic of recommendation. Grade C (evidence level IV): Requires evidence obtained from expert committ reports or opinions and/or clinical experiences of respected authorities. Indicat absence of directly applicable clinical studies of good quality. Good Practice Points: Recommended best practice based on the clinical expe the guideline development group.
ACS (2001)	Not applicable
USPSTF (2002)	The U.S. Preventive Services Task Force (USPSTF) grades its recommendati according to one of five classifications (A, B, C, D, or I), reflecting the strength evidence and magnitude of net benefit (benefits minus harms). **A** The USPSTF strongly recommends that clinicians routinely provide [the servic eligible patients. (The USPSTF found good evidence that [the service] improv important health outcomes and concludes that benefits substantially outweigh **B** The USPSTF recommends that clinicians routinely provide [the service] to elig patients. (The USPSTF found at least fair evidence that [the service] improves outcomes and concludes that benefits outweigh harms.) **C** The USPSTF makes no recommendation for or against routine provision of [th service]. (The USPSTF found at least fair evidence that [the service] can impr health outcomes but concludes that the balance of benefits and harms is too c justify a general recommendation.) **D**

	The USPSTF recommends against routinely providing [the service] to asympt patients. (The USPSTF found at least fair evidence that [the service] is ineffec that harms outweigh benefits.) **I** The USPSTF concludes that the evidence is insufficient to recommend for or a routinely providing [the service]. (Evidence that [the service] is effective is lack poor quality, or conflicting and the balance of benefits and harms cannot be determined.) The U.S. Preventive Services Task Force (USPSTF) grades the **quality of the** **evidence** on a 3-point scale (good, fair, or poor). **Good** Evidence includes consistent results from well-designed, well-conducted studi representative populations that directly assess effects on health outcomes. **Fair** Evidence is sufficient to determine effects on health outcomes, but the strengt evidence is limited by the number, quality, or consistency of the individual stuc generalizability to routine practice; or indirect nature of evidence on health out **Poor** Evidence is insufficient to assess the effects on health outcomes because of li number of power of studies, important flaws in their design or conduct, gaps in chain of evidence, or lack of information on important health outcomes.

TABLE 3: BENEFITS AND HARMS	
POTENTIAL BENEFITS ASSOCIATED WITH PROSTATE CANCER SCREENING	
ACPM (1998 Jul)	Screening potentially could result in decreased morbidity and mortality due to e detection and treatment of prostate cancer. However, there is no direct evidenc whether or not early detection and treatment of prostate cancer reduces mortal because randomized clinical trials to address the question have not been completed. Because screening may be detecting cancers that would never hav caused morbidity or mortality in the host, the value of early detection remains unclear.
AUA (1999)	PSA testing detects more tumors than does DRE and detects them earlier. Alth many of these tumors have aggressive characteristics, some may grow slowly enough that they pose no risk to the patient. As yet, there is no way to identify certainty the tumor that has no risk of spreading and potentially causing prema death or morbidity.
Singapore MOH (2000)	While the incidence of prostate cancer is substantially lower than that in many Western countries, it has been increasing even after having corrected for life expectancy. The majority of patients with prostate cancer present with locally advanced and/or metastatic disease at the time of first diagnosis. The prognos

	advanced prostate cancer is poor despite the most aggressive treatment. Cure impossible for metastatic prostate cancer. The median time to progression and median survival is approximately 18 and 30 months respectively. Such data co sharply with the results of treatment for localized disease where medial surviva been shown to be longer than 15 years. The observed crude survival rates are identical to the expected survival of age-matched controls. As such, it is reasor to strive for early diagnosis and treatment in the hope of survival benefits. How uncertainties of the natural history of the disease and efficacy of treatment due the lack of randomised control studies still cast doubts on the potential benefits screening programme. The combination of DRE and PSA enhances early detection. Clinically significant cancers are detected by PSA testing. PSA-based screenin induced a stage migration, but only very preliminary indications of improved su are available.
ACS (2001)	Prostate cancer screening may result in the diagnosis of earlier-stage disease younger men, which may decrease prostate cancer mortality rates. However, no direct evidence exists to show that prostate-specific antigen (PSA screening decreases prostate cancer mortality rates.
USPSTF (2002)	**Effectiveness of Early Detection** The U.S. Preventive Services Task Force (USPSTF) found one randomized, controlled trial (RCT), and three case-control studies examining the effect of screening on prostate cancer mortality. The single RCT of PSA and DRE scree which reported a benefit from screening, was hampered by a low rate of accep of screening in the intervention group (24%), and by flaws in the published ana no difference in prostate cancer deaths was observed between the groups randomized to screening versus usual care using "intention to treat" analysis. T case-control studies of screening DRE produced mixed results. A number of R of PSA screening for prostate cancer are under way in both the U.S. and Europ but they are not expected to report results for several years. Data are also limited to determine whether and how much treatment of screen-detected cancers improves outcomes. No properly controlled, prospective stud are available to determine whether prostatectomy or radiation, the most comm used treatments for prostate cancer, reduce mortality or are more effective thai "watchful waiting" for organ-confined prostate cancer. Several such trials are currently under way. In observational studies, outcomes are worst, and the pot impact of aggressive treatment greatest, for poorly differentiated cancers. In th absence of better data on which treatments are effective for which tumors, the USPSTF concluded that it could not determine whether the increased detectior prostate cancer from screening would reduce mortality and morbidity. The USPSTF also examined a variety of ecologic data, including studies of sec trends in prostate cancer mortality after introduction of PSA screening and comparisons of prostate cancer mortality rates in communities with and withou screening. Prostate cancer mortality rates in the U.S. have declined since 1991 However, the available ecologic studies have not provided sufficient evidence t prostate cancer trends in the U.S. or other populations are attributable to scree differences in prostate cancer treatment, underlying risk factors, and how deatl

	classified can all introduce bias into ecological comparisons.
POTENTIAL HARMS ASSOCIATED WITH PROSTATE CANCER SCREENING	
ACPM (1998 Jul)	Both screening and treatment can be harmful. A positive DRE and/or PSA requ repeat testing can lead to more invasive diagnostic tests, such as needle biops which carries a small risk of infection, sepsis or bleeding. Radical prostatectom radiation therapy can produce serious complications affecting quality of life suc urinary incontinence, erectile dysfunction, or stricture. Little is known about the individual psychological burden involved in prostate cancer screening and deci making regarding treatment.
AUA (1999)	*Tradeoff associated with improving PSA sensitivity*: Both age-adjusted PSA an PSA velocity will increase the number of cancers detected, but both will also increase the number of men undergoing biopsy. *Tradeoff associated with improving PSA specificity*: All three methods to improv PSA specificity (age-adjusted PSA, free-to-total PSA ratio, PSA density) will re the number of biopsies in men who do not have prostate cancer but will increas risk that some prostate cancers will be missed. *Complications of confirmatory testing*: Prostate biopsy by means of a transrecta ultrasound guide, are rarely complicated by rectal bleeding, hematuria, or prost infection. After biopsy, blood in the stool or urine usually disappears in a few da Blood in the semen can be seen for up to several weeks after biopsy.
Singapore MOH (2000)	Not stated
ACS (2001)	Since prostate-specific antigen is prostate-tissue specific and not prostate-canc specific, there is no absolute value that is applicable to all men. The range of "normal" prostate-specific antigen levels has conventionally been considered to between zero and 4.0 ng/ml. A lower cut-off value of 2.5 ng/ml has been shown improve the early detection of organ-confined prostate cancers; however, this a increases the number of men undergoing biopsy in whom no cancer is detecte
USPSTF (2002)	Evidence about the harms of screening *per se* is scant. The screening process likely associated with some increase in anxiety, but the number of men affecte the magnitude of the increased anxiety are largely unknown. Some screening procedures cause transient discomfort. Fewer than 10% of men have ongoing interference with daily activities after biopsy, and fewer than 1% suffer more se complications, including infections. Screening may result in harm if it leads to treatments that carry side effects wit improving outcomes from prostate cancer, especially for cancers that have a lo chance of progressing. Erectile dysfunction, urinary incontinence, and bowel dysfunction are well-recognized and relatively common adverse effects of treat with surgery, radiation or androgen ablation, but men differ in their responses t these symptoms.

GUIDELINE CONTENT COMPARISON

The American College of Preventive Medicine (ACPM), the American Urological Association (AUA), the Singapore Ministry of Health (MOH), the American Cancer Society (ACS), and the U.S. Preventive Services Task Force (USPSTF) present recommendations for screening men for prostate cancer and provide explicit reasoning behind their judgments.

The guideline from the Singapore MOH provides recommendations for diagnosis, treatment, and management of prostate cancer in addition to the recommendations for screening for the disease. The focus of the AUA guideline is PSA and recommendations are provided for the use of this test in screening, pretreatment staging and post-treatment management of men with prostate cancer.

The Singapore MOH guideline targets Asian men whereas the ACPM, AUA, ACS, and USPSTF guidelines target American men.

Areas of Agreement

Routine screening
All five organizations cite the lack of proof that screening can reduce mortality from prostate cancer. ACPM, AUA, Singapore MOH and ACS recommend against routine screening; USPSTF does not recommend for or against routine screening. In addition, ACPM, AUA, ACS and USPSTF address the clear potential that screening will increase treatment-related morbidity. For the American male population, ACPM is more explicit about not recommending population-based screening than AUA, ACS and USPSTF. The Singapore MOH is explicit in their recommendations against routine prostate cancer screening in Asian males.

Targeted screening/Informed decision-making
As the incidence of prostate cancer increases with age, ACPM, AUA, ACS and USPSTF generally recommend that screening should be offered to men 50 years of age and older with at least a 10 year life expectancy and men less than 50 years of age at risk for developing prostate cancer. These four organizations assert that men should make an informed decision regarding prostate cancer screening with the help of their physicians. Singapore MOH suggests that all males be considered for prostate screening who are above 40 years of age at risk for developing prostate cancer.

Screening tests
When the decision to screen is made, there is agreement among the groups that PSA and DRE are the primary screening tests for prostate cancer.

The use of transrectal ultrasound as a screening test for prostate cancer is no longer considered by ACPM or USPSTF and the AUA recommends against it. ACS mentions this test once in their guideline in terms of biopsy, and similarly, the Singapore MOH does not address transrectal ultrasound as a screening test, but rather consider it in combination with biopsy for diagnostic purposes.

Areas of Differences

Screening tests

Although there is agreement among all the groups on the use of PSA and DRE as the primary screening tools for prostate cancer, AUA, Singapore MOH and ACS explicitly recommend combining the two to improve accuracy. ACPM notes the increased positive predictive value of combining the tests, but makes no recommendation about the combination. The USPSTF notes that when DRE and PSA are combined more cancers are detected than PSA alone but does not recommend the combination because increased detection would be offset by an increase in false-positive results.

There is variation among the five organizations regarding the best methods to improve PSA sensitivity and specificity. All agree that a PSA threshold level of 4.0 ng/ml will detect many cancers but that as many as 10% to 20% may be missed. AUA and ACPM discuss methods such as age-adjusted PSA and PSA velocity to improve sensitivity and age adjustment, free-to-total PSA ratios and PSA density to improve specificity. ACS discusses age-specific reference ranges, PSA density, and free-to-total PSA ratios, suggesting the latter method be used to increase testing accuracy in certain scenarios. Singapore MOH does not recommend age-specific ranges or PSA density, and states PSA velocity is probably not useful. This group does recommend use of free-to-total PSA levels, noting however that optimal cut off is still being investigated, and overall, the value of PSA testing in Asian men is not as clear as it is in Western populations. Finally, USPSTF does not recommend any of these methods noting that there is insufficient evidence that these variations will improve the accuracy of screening in practice.

Frequency of targeted screening

ACS is the only group that specifically recommends annual screening for men over 50 and younger men at increased risk. In contrast, USPSTF reports that cancer detection declines rapidly with repeated annual testing and suggests biennial screening as equally effective, if screening were to reduce mortality. ACPM, MOH and AUA do not address the issue of how often screening should be performed.

This Synthesis was prepared by NGC on December 28, 1998 and revised to include additional guideline developers on April 18, 2000. It was reviewed by the guideline developers as of June 27, 2000. Updated recommendations issued by the American Cancer Society (ACS) were incorporated into this synthesis by NGC on April 20, 2001 and were reviewed by the guideline developer as of August 28, 2001. This Synthesis was updated on March 15, 2002 to incorporate Singapore MOH guidelines. Recommendations from USPSTF and Canadian Task Force on Preventive Health Care (CTFPHC) were also removed from this Synthesis following their withdrawal from the NGC Web site. This Synthesis was updated most recently on December 10, 2002 to incorporate updated recommendations issued by the USPSTF.

Internet citation: National Guideline Clearinghouse (NGC). Guideline synthesis: Screening for prostate cancer. In: National Guideline Clearinghouse (NGC) [website]. Rockville (MD): 1998 Dec 28 (updated 2003 Jan 3). [cited YYYY Mon DD]. Available: http://www.guideline.gov.

Date Modified: 12/13/2004